

# Diethylene Glycol Monoethyl Ether Versus Propylene Glycol And Their Impact On Topical Clobetasol Propionate Drug Delivery

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## INTRODUCTION

Propylene Glycol (PG) is an aliphatic alcohol product of propylene oxide and water, widely used as a solvent and viscosity decreasing agent in cosmetic formulations. *In vitro* data have shown a positive correlation between PG concentration in topical pharmaceutical formulations and degree of drug penetration. Diethylene glycol monoethyl ether (DEGEE - Transcutol®, Gattefossé) is a permeation enhancer also employed in topical pharmaceuticals proven to increase penetration and drug retention within the skin due to its broad range of hydrophilic and lipophilic actives.<sup>1</sup> DEGEE is found as an excipient in a novel formulation of clobetasol propionate 0.025% cream (CPD – Impoyz®, Primus Pharmaceuticals), proven to promote lower plasma drug concentrations and less hypothalamic-pituitary-adrenal suppression as compared to clobetasol propionate 0.05% cream containing PG (CPPG - Temovate®, Fougera Pharmaceuticals).<sup>2</sup> In a Phase II clinical trial of patients with moderate to severe plaque psoriasis randomized to CPD or CPPG, both the mean plasma drug concentration and the proportion of patients with an abnormal adrenocorticotrophic hormone (ACTH) level at day 15 in those receiving CPD were one-third of that observed in those treated with CPPG (with one-half expected), suggesting a role for DEGEE in maintaining drug within the skin with less systemic absorption.<sup>3</sup> As different enhancers may promote drug delivery through the skin and into systemic circulation with disparity, we examined the relative permeation of CPPG compared to CPD through an *in vitro* human skin permeation (IVHSP) model. In a separate experiment, we measured the relative amount of PG found in clobetasol propionate containing comparator steroid creams (CSC's).

## OBJECTIVE

**Study 1:** To investigate the relative absorption of CPPG versus CPD.

**Study 2:** To assess the amount (weight %) of PG in CSC's.

### DISCLOSURES:

**LK**  
**Speaker:** Abbott, Allergan, Ammirall, Amgen, CIPHER, Connetics, Dermavant, Dermira, Eli Lilly, Galderma, Genentech, GSK, J&J, Leo, Maruho, PharmDerm, Serono, Stiefel Laboratories, Sun Pharma, Taro, UCB, Valeant  
**Consultant:** Abbvie, Allergan, Ammirall, Amgen, Arcutis, BMS, CIPHER, Connetics, Dermavant, Dermira, Dr. Reddy's Lab, Eli Lilly, Galderma, Genentech, GSK, J&J, Leo, Merck, Novartis AG, Primus Pharmaceuticals, Promius, Stiefel Laboratories, Sun Pharma, Taro, UCB, Valeant  
**Investigator:** Abbvie, Allergan, Ammirall, Amgen, Arcutis, BMS, Boehringer-Ingelheim, Breckenridge Pharma, Celgene, Centocor, Cellceutix, Combinatrix, Connetics, Coria, Dermavant, Dermira, Dow Pharmaceutical Sciences, Dr. Reddy's Lab, Eli Lilly, Galderma, Genentech, GSK, Idera, J&J, Leo, Maruho, Merck, Medicis Pharmaceutical Corp, Novartis AG, Promius, PharmaDerm, Pfizer, Stiefel Laboratories, Sun Pharma, UCB, Valeant, Xenoport  
**Advisory Board:** Allergan, Ammirall, Amgen, Arcutis, Biogen-Idex, BMS, Celgene, CIPHER, Connetics, Dermavant, Dermira, Dr. Reddy's Lab, Eli Lilly, Galderma, Genentech, GSK, J&J, Promius, Stiefel Laboratories, Sun Pharma, Valeant  
**RH, GC and EH**  
Employees of Primus Pharmaceuticals

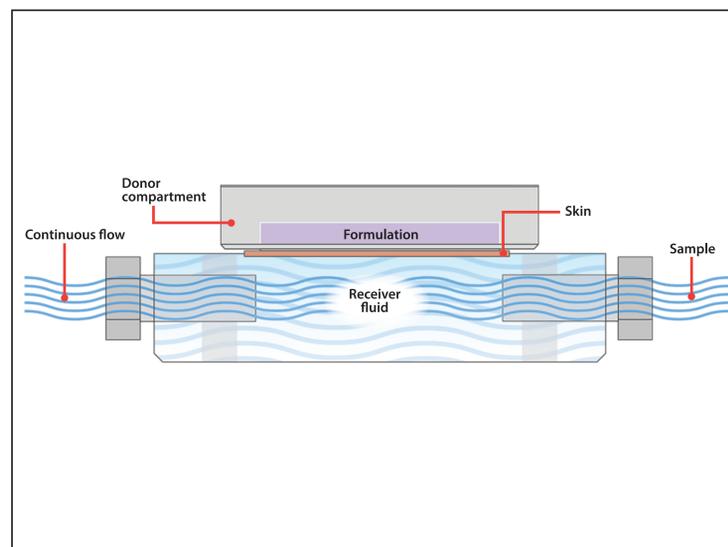
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## METHODS

**Study 1:** IVHSP testing employed the MedFlux-HT™ system (Figure 1) to evaluate drug permeation and clobetasol propionate releasing profiles using three skin donors. Statistical methods included a one-way analysis of the log-transformed mean cumulative amount of clobetasol propionate permeating through a 1 cm<sup>2</sup> skin dosing area by formulation using Tukey-Kramer.

**Study 2:** Three samples of CSC's were submitted for the determination of PG content by gas chromatography-mass spectrometry. A calibration curve from analysis of PG reference solutions was used to calculate the amount of PG in each sample.

**Figure 1.**  
MedFlux™ Diffusion Cell



## RESULTS

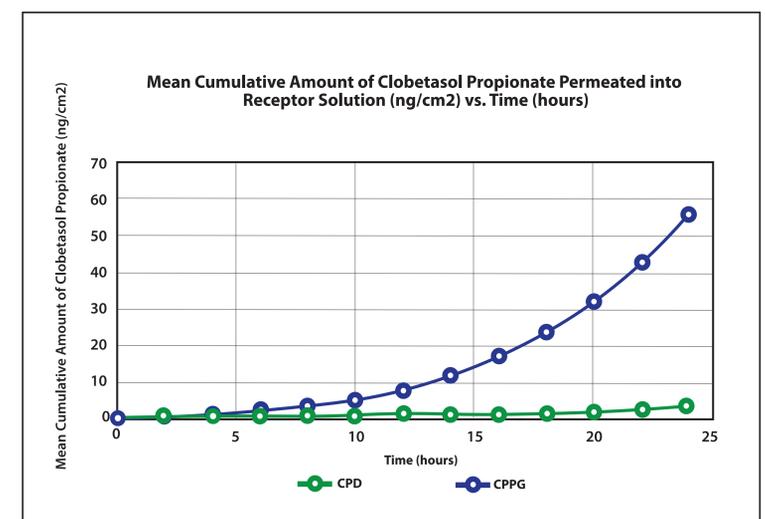
**Study 1:** The mean cumulative amount of clobetasol propionate delivered to the receptor solution at 24 hours was statistically greater ( $P < 0.05$ ) for CPPG than CPD, at 56.39 ng/cm<sup>2</sup> and 3.28 ng/cm<sup>2</sup>, respectively. (Figure 2) Thus, the amount of clobetasol propionate that passed through the skin one day following application of the product containing PG is 17 times that of the product employing a DEGEE vehicle.

**Study 2:** The tested CSC's were comprised of a range between 42.5 to 50.8% PG by weight. (Table 1)

## CONCLUSIONS

Clobetasol propionate containing comparator steroid creams contain high propylene glycol (PG) concentrations, increasing the degree of clobetasol permeation through the skin and potential of passage into systemic circulation. A novel formulation of clobetasol propionate 0.025% cream containing diethylene glycol monoethyl ether (DEGEE) exhibits low transcutaneous permeation of corticosteroid with less risk of systemic delivery and HPA axis suppression.

**Figure 2.**  
Accumulation of Clobetasol Propionate Formulations in Receptor Fluid Over Time



**Table 1.**  
Topical Clobetasol Propionate Comparator Products - Propylene Glycol Content

Sample I.D.	Weight % PG
P211048-1	47.7%
P211048-2	50.8 %
P211048-3	42.5 %

## REFERENCES

- Osborne DW, Musakhanian J. Skin Penetration and Permeation Properties of Transcutol®-Neat or Diluted Mixtures. *AAPS PharmSciTech* 2018;19(8):3512-3533.doi:10.1208/s12249-018-1196-8
- Del Rosso JQ. Topical Corticosteroid Therapy for Psoriasis-A Review of Clobetasol Propionate 0.025% Cream and the Clinical Relevance of Penetration Modification. *J Clin Aesthetic Dermatol.* 2020;13(2):22-29.
- Draeos ZD, Fowler JF, Cornelison R. A Randomized, Parallel Group, Open Label, Multicenter Study to Assess the Potential for Adrenal Suppression and Systemic Drug Absorption Following Multiple Dosing with Clobetasol Propionate Cream (Impoyz®), 0.025% versus Clobetasol Propionate (Temovate®) Cream, 0.05% in Subjects with Moderate to Severe Plaque Psoriasis. *Skin.* 2018;2(6): 410-420.



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